

**Abstract**

The present invention relates to nucleic acid molecules related to the *PFD1235w/MAL7P1.1*, *PF11\_0008*, and *PF13\_0003* gene families as well as amino acid sequences encoded by such nucleic acid molecules with respect to their role in mediating

5 adhesion of infected red blood cells to endothelial cells, which is characteristic for the pathogenesis of severe malaria (SM). Accordingly, the invention provides pharmaceutical compositions and vaccines, hereunder nucleotide-based vaccines comprising compounds that are related to VAR4, VAR5, and/or VAR6 polypeptides and *PFD1235w/MAL7P1.1*, *PF11\_0008*, and/or *PF13\_0003* nucleic acid molecules. The invention further relates to the

10 use of these compounds as medicaments and for the manufacture of compositions, such as immunogenic compositions. In addition, the invention relates to methods of treatment and prevention of severe malaria wherein these methods are based on the nucleic acid molecules and polypeptides of the invention. As these compounds can also be used as biotechnological tools the invention provides *in vitro* diagnostic methods and kits

15 comprising reagents and IgGs/antibodies designated to the use in such methods. The invention also relates to methods of identifying agents capable of modulating the VAR4, VAR5, and/or VAR6 dependent adhesion to endothelial cells and agent capable of interacting with VAR4, VAR5, and/or VAR6. Finally, a method for identifying polypeptides, which will induce a specific IgG/ antibody response upon administration to a subject is

20 provided by the invention.